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10/004,645	12/04/2001	Satoh Yoshitaka	10624-050-999	6771

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EXAMINER
KIM, JENNIFER M

ART UNIT	PAPER NUMBER
1617	10

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/004,645	Applicant(s) YOSHITAKA ET AL.	
	Examiner Jennifer Kim	Art Unit 1617	

-- The MAILING DATE of this c mmunication appears n the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *2,3,6-16 and 19-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,17,18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election with traverse of Group II, claims 1, 4, 5, 17 and 18, drawn to a method for treating a cardiovascular, metabolic or ischemic condition comprising administering a compound having the structure set forth in claims 1 and 17 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that a search related to methods for treatment comprising the administration of the compounds of the present claims would not impose an undue burden on the Examiner. This is not found persuasive because the claims are drawn to patentably distinct and independent medical disorders having different etiology. Therefore the required literature search would place extreme burden on the Examiner. Therefore, the restriction requirement as indicated in the last Office Action is deemed proper and made Final.

The claims have been examined only to the extent of Applicants' election. C1aims 2, 3, 6-16, 19-26 are withdrawn from consideration since they are non-elected invention.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 4 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treatment of the specific cardiovascular, metabolic or ischemic condition", does not reasonably provide enablement for the treatment of **any** cardiovascular, metabolic or ischemic condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method of treating **a condition** (cardiovascular, metabolic or ischemic condition) responsive to inhibition of the JNK pathway, comprising administering to a subject an effective amount of a compound set forth in claims 1 and 17. The nature of the invention is extremely complex in that it encompasses the actual treatment of **a condition** of cardiovascular, metabolic or ischemic condition (i.e. any of cardiovascular (e.g. hypertension, CHF etc.), any of metabolic (e.g. obesity, indigestion), any of ischemic condition (e.g. aneurysm, hypoxia) such that the subject suffering from **any of cardiovascular, metabolic or ischemic**

conditions would receive beneficial therapeutic treatment from claimed compounds.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass treatment of **a condition** (cardiovascular, metabolic or ischemic condition) responsive to inhibition of the JNK pathway, in a subject which has potentially many different causes (i.e. many different mechanisms or combination of mechanisms). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually treat **any condition** (cardiovascular, metabolic or ischemic condition) responsive to inhibition of the JNK pathway, comprising administering to a subject an effective amount of a compound set forth in claims 1 and 17 is minimal. All of the guidance provided by the specification is directed towards treatment of specific cardiovascular, metabolic or ischemic conditions rather than the treatment of any cardiovascular, metabolic or ischemic conditions.

Working Examples: All of the working examples provided by the specification are directed toward the treatment of specific cardiovascular, metabolic or ischemic conditions rather than treatment of any of cardiovascular, metabolic or ischemic conditions.

State of the Art: While the state of the art is relatively high with regard to treatment of specific cardiovascular, metabolic or ischemic, the state of the art

with regard to treatment of any of such disorders is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject for the treatment of any of cardiovascular, metabolic or ischemic disorders.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual treatment of any of cardiovascular, metabolic or ischemic in a subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of treatment of any cardiovascular, metabolic or ischemic disorders responsive to inhibition of the JNK pathway.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for the treatment of any of cardiovascular, metabolic or ischemic disorders. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard to treatment of any of cardiovascular, metabolic or ischemic disorders with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model

system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding treatment of any of cardiovascular, metabolic or ischemic disorders with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat any of cardiovascular, metabolic or ischemic disorders in a subject by administration of one of the claimed compounds.

Therefore, a method of treating **any cardiovascular, metabolic or ischemic disorders** responsive to inhibition of the JNK pathway in a subject administering compounds set forth in claims 1 and 17 is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 5, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Torley et al. (U.S.Patent No. 4,879,252) of record.

Torley et al. teach that Applicants' active agents are useful for the treatment of diabetes in mammal. (column 2, lines 14-17, Examples 265, 266).

Applicants' recitation in claims of the mechanism of inhibiting the JNK pathway by which the active ingredient gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same. An explanation of why that effect occurs does not make novel the treatment of the conditions encompassed by the claims.

Claims 1, 4, 5, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al. (U.S.Patent No. 6,114,333).

Davis et al. teach that Applicants' active agents are useful for the treatment of graft v host disease and transplantation associated rejection events. (abstract, column 7, line 58 through column 8, line 6).

Applicants' recitation in claims of the mechanism of inhibiting the JNK pathway by which the active ingredient gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same. An explanation of why that effect occurs does not make novel the treatment of the conditions encompassed by the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,4,5, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (U.S.Patent No. 6,114,333) in view of Murata et al. (U.S.Patent No. 6,361,760B1) and further in view of Adam et al. (1999).

Davis et al's teaching as applied as before and additional teachings as follow:

Davis et al. teach that Applicants' active agents are useful for the prophylaxis and treatment of thrombosis of the major organs. (abstract, column 7, line 58 through column 8, line 6).

Davis et al. do expressly teach the treatment of ischemic diseases of specific organs of kidney, liver and brain, myocardial infarction and multiple organ failure.

Murata et al. disclose that thrombosis is an ischemic disease. (column 10, lines 38-39).

Adam et al. teach that thrombosis leads to myocardial infarction and multiple organ failure.

It would have been obvious to one of ordinary skill in the art to employ the active agents in the treatment of ischemic diseases of specific organs set forth in claim 5 because Davis et al. teach that the active agents are useful for the prophylaxis and treatment of thrombosis of the major organs and because thrombosis and myocardial infarction are the type of ischemic disease and particularly, myocardial infarction is the ischemic disease of major organ (i.e. heart). One would have been motivated to employ the active agents for the treatment of ischemic diseases of specific organs set forth in claim 5 to achieve therapeutic benefit of preventing ischemic condition (i.e. thrombosis) of major organs (e.g. heart (myocardial infarction), kidney, liver and brain) as taught by

David et al. Moreover, multiple organ failure would be obviously treated upon the treatment of ischemic disease (e.g. thrombosis) as modified above since the thrombosis leads to multiple organ failure. Applicants' recitation in claims of the mechanism of inhibiting the JNK pathway by which the active ingredient gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same. An explanation of why that effect occurs does not make novel the treatment of the conditions encompassed by the claims.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 703-308-2232. The examiner can normally be reached on Monday through Friday 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 703-305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

9/8/03

jmk
August 29, 2003